```
      ---  -----  -----------
? s accept? (5n) hydrophobic (5n)carrier
          163135  ACCEPT?
           20961  HYDROPHOBIC
          209851  CARRIER
      S1      50  ACCEPT? (5N) HYDROPHOBIC (5N)CARRIER
? s cell(5n)membrane
          174645  CELL
           50838  MEMBRANE
      S2    4918  CELL(5N)MEMBRANE
? s s1 and s2
              50  S1
            4918  S2
      S3      20  S1 AND S2
? s pass? or cross?
          785726  PASS?
          411614  CROSS?
      S4 1083142  PASS? OR CROSS?
? s s3 and s4
              20  S3
         1083142  S4
      S5      20  S3 AND S4
? t s5/3,k,ab/1-20

 5/3,K,AB/1
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2004 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 10421642  IFI Acc No: 2003-0166066  IFI Acc No: 2003-0049111
Document Type: C
DNA ENCODING A HUMAN SEROTONIN RECEPTOR (5-HT4B) AND USES THEREOF
Inventors: Bard Jonathan A (US); Branchek Theresa (US); Weinshank Richard L
    (US)
Assignee: Synaptic Pharmaceutical Corp
Assignee Code: 34644
Publication (No,Date), Applic (No,Date):
US 20030166066 20030904 US 2002118804  20020409
Publication Kind:  A1
Continuation Pub(No),Applic(No,Date): US 5985585                US 95157185
  19950615; US 6432655                US 99332837     19990614
Section 371 Pub(No,Date),Applic(No,Date):US 95157185    19950615;WO
93US10553   19931029
Priority Applic(No,Date): US 2002118804  20020409; US 95157185    19950615;
US 99332837    19990614

Abstract: This invention provides an isolated nucleic acid encoding a
mammalian 5-HT4B  receptor and an isolated nucleic acid encoding a human
5-HT4B receptor, an isolated protein which is a mammalian 5-HT4B receptor,
vectors comprising an  isolated nucleic acid encoding a mammalian 5-HT4B
receptor, mammalian cells  comprising such vectors, antibodies directed to
the 5HT4B receptor, nucleic  acid probes useful for detecting nucleic acid
encoding a mammalian or human  5-HT4B receptor, antisense oligonucleotides
complementary to any sequences of a nucleic acid which encodes a mammalian
or human 5-HT4B receptor, and pharmaceutical compounds related to the human
5-HT4B receptor. This invention further provides methods for determining
ligand binding, detecting  expression, drug screening, and treatments for
alleviating abnormalities associated with a human 5-HT4B receptor.


Non-exemplary Claims: ...oligonucleotide of claim 24 effective to reduce
   expression of a human 5-HT4B  receptor by passing through a
   cell membrane and specifically binding with mRNA encoding a
   human 5-HT4B receptor in the cell so as to prevent its translation and a
    pharmaceutically acceptable hydrophobic carrier
```

capable of **passing** through a **cell membrane**.
...

...53. A pharmaceutical composition of claim 51, wherein the pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane** comprises a structure which binds to a transporter specific for a selected cell type and...mammal, which plasmid further comprises DNA which expresses a human 5-HT4B receptor on the **cell**'s surface, isolating a **membrane** fraction from the **cell** extract, incubating the compound with the membrane fraction under conditions permitting binding of ligands known...

...cell which plasmid further comprises DNA which expresses a human 5-HT4B receptor on the **cell**'s surface, isolating a **membrane** fraction from the **cell** extract, incubating the **membrane** fraction with a plurality of compounds, determining those compounds which interact with and bind to...

5/3,K,AB/2
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10369354 IFI Acc No: 2003-0113772 IFI Acc No: 2003-0032438
Document Type: C
DNA ENCODING HUMAN ALPHA 1 ADRENERGIC RECEPTORS AND USES THEREOF
Inventors: Bard Jonathan A (US); Forray Carlos C (US); Weinshank Richard L (US)
Assignee: Synaptic Pharmaceutical Corp
Assignee Code: 34644
Publication (No,Date), Applic (No,Date):
US 20030113772 20030619 US 2002238667 20020910
Publication Kind: A1
Continuation Pub(No),Applic(No,Date): US 6083705 US 98206899 19981207; US 6156518 US 99474551 19991229; US 6448011 US 2000688415 20001016
Cont.-in-part Pub(No),Applic(No,Date): US 92952798 19920925
Division Pub(No),Applic(No,Date): US 5861309 US 95406855 19950821
Priority Applic(No,Date): US 2002238667 20020910; US 98206899 19981207; US 99474551 19991229; US 2000688415 20001016; US 92952798 19920925; US 95406855 19950821
Abstract: This invention provides an isolated nucleic acid, vectors, transformed mammalian cells and non-human transgenic animals that encode and express normal or mutant alpha 1a, alpha 1b and alpha 1c adrenergic receptor genes. This invention also provides a protein, and an antibody directed to the protein and pharmaceutical compounds related to alpha 1a, alpha 1b and alpha 1c adrenergic receptors. This invention provides nucleic acid probes, and antisense oligonucleotides complementary to alpha 1a, alpha 1b and alpha 1c adrenergic receptor genes. This invention further provides methods for determining ligand binding, detecting expression, drug screening, and treatments for alleviating abnormalities associated with human alpha 1a, alpha 1b and alpha 1c adrenergic receptors.

Non-exemplary Claims: ...of claim 27 effective to reduce expression of a human alpha 1a adrenergic receptor by **passing** through a **cell membrane** and specifically binding with mRNA encoding a human alpha 1a adrenergic receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.
...

...of claim 28 effective to reduce expression of a human alpha 1b adrenergic receptor by **passing** through a **cell membrane** and specifically binding with mRNA encoding a human alpha 1b adrenergic receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier**.
...

...of claim 29 effective to reduce expression of a human alpha 1c adrenergic receptor by **passing** through a **cell membrane** and specifically binding with mRNA encoding a human alpha 1c adrenergic receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier**.
...

...63. A pharmaceutical composition of claim 61, wherein the pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane** comprises a structure which binds to a transporter specific for a selected cell type and...further comprise a DNA molecule which expresses a human alpha 1 adrenergic receptor on the **cell** surface, isolating a **membrane** fraction from the **cell** extract, incubating the ligand with the membrane fraction under conditions permitting binding of ligands known...further comprise a DNA molecule which expresses a human alpha 1 adrenergic receptor on the **cell** surface, isolating a **membrane** fraction from the **cell** extract, incubating the **membrane** fraction with a plurality of drugs, determining those drugs which interact with and bind to...and activating or inhibiting a human alpha 1 adrenergic receptor, which comprises contacting a mammalian **cell**, wherein the **membrane** lipids have been labelled by prior incubation with a labelled myo-inositol phosphate molecule, the...

5/3,K,AB/3
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10369353 IFI Acc No: 2003-0113771 IFI Acc No: 2003-0032437
Document Type: C
DNA ENCODING HUMAN ALPHA 1 ADRENERGIC RECEPTORS AND USES THEREOF
Inventors: Bard Jonathan A (US); Forray Carlos C (US); Weinshank Richard L (US)
Assignee: Synaptic Pharmaceutical Corp
Assignee Code: 34644
Publication (No,Date), Applic (No,Date):
US 20030113771 20030619 US 2002238129 20020910
Publication Kind: A1
Continuation Pub(No),Applic(No,Date): US 6083705 US 98206899 19981207; US 6156518 US 99474551 19991229; US 6448011 US 2000688415 20001016
Cont.-in-part Pub(No),Applic(No,Date): US 92952798 19920925
Division Pub(No),Applic(No,Date): US 5861309 US 95406855 19950821
Priority Applic(No,Date): US 2002238129 20020910; US 98206899 19981207; US 99474551 19991229; US 2000688415 20001016; US 92952798 19920925; US 95406855 19950821
Abstract: This invention provides an isolated nucleic acid, vectors, transformed mammalian cells and non-human transgenic animals that encode and express normal or mutant alpha 1a, alpha 1b and alpha 1c adrenergic receptor genes. This invention also provides a protein, and an antibody directed to the protein and pharmaceutical compounds related to alpha 1a, alpha 1b and alpha 1c adrenergic receptors. This invention provides

nucleic acid probes, and antisense oligonucleotides complementary to alpha 1a, alpha 1b and alpha 1c adrenergic receptor genes. This invention further provides methods for determining ligand binding, detecting expression, drug screening, and treatments for alleviating abnormalities associated with human alpha 1a, alpha 1b and alpha 1c adrenergic receptors.

Non-exemplary Claims: ...of claim 27 effective to reduce expression of a human alpha 1a adrenergic receptor by **passing** through a **cell membrane** and specifically binding with mRNA encoding a human alpha 1a adrenergic receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.
...

...of claim 28 effective to reduce expression of a human alpha 1b adrenergic receptor by **passing** through a **cell membrane** and specifically binding with mRNA encoding a human alpha 1b adrenergic receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier**.
...

...of claim 29 effective to reduce expression of a human alpha 1c adrenergic receptor by **passing** through a **cell membrane** and specifically binding with mRNA encoding a human alpha 1c adrenergic receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier**.
...

...63. A pharmaceutical composition of claim 61, wherein the pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane** comprises a structure which binds to a transporter specific for a selected cell type and...further comprise a DNA molecule which expresses a human alpha 1 adrenergic receptor on the **cell** surface, isolating a **membrane** fraction from the **cell** extract, incubating the ligand with the membrane fraction under conditions permitting binding of ligands known...further comprise a DNA molecule which expresses a human alpha 1 adrenergic receptor on the **cell** surface, isolating a **membrane** fraction from the **cell** extract, incubating the **membrane** fraction with a plurality of drugs, determining those drugs which interact with and bind to...and activating or inhibiting a human alpha 1 adrenergic receptor, which comprises contacting a mammalian **cell**, wherein the **membrane** lipids have been labelled by prior incubation with a labelled myo-inositol phosphate molecule, the...

5/3,K,AB/4
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10324783 IFI Acc No: 2003-0069197 IFI Acc No: 2003-0018893
Document Type: C
PITUITARY-TUMOR-TRANSFORMING-GENES, AND RELATED PRODUCTS
Inventors: Melmed Shlomo (US); Pei Lin (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20030069197 20030410 US 2002163277 20020604
Publication Kind: A1
Continuation Pub(No),Applic(No,Date): PENDING US 99894251 19990723
Section 371 Pub(No,Date),Applic(No,Date):US 99894251 19990723;WO

97US21463 19971121
Priority Applic(No,Date): US 2002163277 20020604; US 99894251 19990723
Provisional Applic(No,Date): US 60-31338 19961121

Abstract: PTTG polypeptides are expressed by the pituitary-tumortransforming-gene (PTTG), formerly known as pituitary-tumorspecific-gene (PTSG), and nucleic acids encode them. Examples are the human and rat PTTG proteins. The nucleic acids may be applied to a method of producing PTTG polypeptide, and to the detection of the presence of PTTG genes in different species. The nucleic acids may be operatively linked to a vector, optionally provided with control and expression sequences and/ or be carried by a recombinant host cell. PTTG oligonucleotide probes and primers are disclosed, which can be employed in diagnostic kits, in methods of identifying or isolating mammalian PTTG nucleic acid, and in a method for detecting a pathological mass associated with PTTG expression. An antisense oligonucleotide is disclosed. Compositions comprising PTTG nucleic acids are also disclosed.

Non-exemplary Claims: ...8. The composition of claim 7, comprising a pharmaceutically **acceptable hydrophobic carrier** that enables the antisense oligonucleotide to **pass** through a **cell membrane**.

5/3,K,AB/5
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10305383 IFI Acc No: 2003-0049794 IFI Acc No: 2003-0013417
Document Type: C
DNA ENCODING A HUMAN DOPAMINE D1 RECEPTOR AND USES THEREOF; NUCLEOTIDE SEQUENCES CODING PROTEIN FOR USE IN THE TREATMENT AND PREVENTION OF NERVOUS SYSTEM, DYSKINESIA, KIDNEY, VASCULAR, CIRCADIAN RHYTHMS AND VISION DEFECTS
Inventors: Hartig Paul R (US); Weinshank Richard L (US)
Assignee: Synaptic Pharmaceutical Corp
Assignee Code: 34644
Publication (No,Date), Applic (No,Date):
US 20030049794 20030313 US 2002277078 20021021
Publication Kind: A1
Continuation Pub(No),Applic(No,Date): US 6468767 US 98168510 19981008
Division Pub(No),Applic(No,Date): US 5882855 US 93969267 19931005
Section 371 Pub(No,Date),Applic(No,Date):US 93969267 19931005;WO 91US4858 19910710
Priority Applic(No,Date): US 2002277078 20021021; US 98168510 19981008; US 93969267 19931005

Abstract: This invention provides isolated nucleic acid molecules encoding a human dopamine D1 receptor, isolated proteins which are human dopamine D1 receptor, vectors comprising isolated nucleic acid molecules encoding a human dopamine D1 receptor, mammalian cells comprising such vectors, antibodies directed to a human dopamine D1 receptor, nucleic acid probes useful for detecting nucleic acid encoding human dopamine D1 receptor, antisense oligonucleotides complementary to any sequences of a nucleic acid molecule which encodes a human dopamine D1 receptor, pharmaceutical compounds related to human dopamine D1 receptor, and nonhuman transgenic animals which express DNA a normal or a mutant human dopamine D1 receptor. This invention further provides methods for determining ligand binding, detecting expression, drug screening, and treatment involving a human dopamine D1 receptor.

Non-exemplary Claims: ...oligonucleotide of claim 28 effective to reduce expression of a human dopamine D1 receptor by **passing** through a **cell membrane** and binding specifically with mRNA encoding a human dopamine D1 receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.

...

...34. A pharmaceutical composition of claim 31, wherein the pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane** comprises a structure which binds to a receptor specific for a selected cell type and

5/3,K,AB/6

Dialog Acc No: 10264421 IFI Acc No: 2003-0008823 IFI Acc No: 2003-0002259
Document Type: C

DNA ENCODING A HUMAN 5-HT1F RECEPTOR AND USES THEREOF; FOR DETERMINING LIGAND BINDING, DETECTING EXPRESSION, DRUG SCREENING, AND TREATMENT INVOLVING THE HUMAN 5-HT1F RECEPTOR

Inventors: Branchek Theresa (US); Hartig Paul R (US); Weinshank Richard L (US)
Assignee: Synaptic Pharmaceutical Corp
Assignee Code: 34644

Publication (No,Date), Applic (No,Date):
US 20030008823 20030109 US 2002166101 20020610
Publication Kind: A1
Continuation Pub(No),Applic(No,Date): US 5639652 US 94117006 19940822; ABANDONED US 95483222 19950607; US 6406859 US 99246075 19990205
Cont.-in-part Pub(No),Applic(No,Date): US 5360735 US 92817920 19920108
Section 371 Pub(No,Date),Applic(No,Date):US 94117006 19940822;WO 93US149 19930108
Priority Applic(No,Date): US 2002166101 20020610; US 94117006 19940822; US 95483222 19950607; US 99246075 19990205; US 92817920 19920108

Abstract: This invention provides an isolated nucleic acid molecule encoding a human 5-HT1F receptor, an isolated protein which is a human 5-HT1F receptor, vectors comprising an isolated nucleic acid molecule encoding a human 5-HT1F receptors. mammalian cells comprising such vectors, antibodies directed to the human 5-HT1F receptor, nucleic acid probes useful for detecting nucleic acid encoding human 5-HT1F receptors, antisense oligonucleotides complementary to any sequences of a nucleic acid molecule which encodes a human 5-HT1F receptor, pharmaceutical compounds related to human 5-HT1F receptors, and nonhuman transgenic animals which express DNA a normal or a mutant human 5-HT1F receptor. This invention further provides methods for determining ligand binding, detecting expression, drug screening, and treatment involving the human 5-HT1F receptor.

Non-exemplary Claims: ...oligonucleotide of claim 19 effective to reduce expression of a human 5-HT1F receptor by **passing** through a **cell membrane** and binding specifically with mRNA encoding a human 5-HT1F receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.

...

...27. A pharmaceutical composition of claim 24, wherein the

pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane** comprises a structure which binds to a receptor specific for a selected cell type and

5/3,K,AB/7
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10248936 IFI Acc No: 2002-0192643 IFI Acc No: 2002-0049786
Document Type: C
NOVEL CARD PROTEINS INVOLVED IN CELL DEATH REGULATION; NUCLEOTIDE SEQUENCES CODING POLYPEPTIDE FOR USE IN THE TREATMENT OF CELL PROLIFERATION OR INFLAMMATORY DISORDERS
Inventors: REED JOHN C (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20020192643 20021219 US 99388221 19990901
Publication Kind: A1
Priority Applic(No,Date): US 99388221 19990901

Abstract: The present invention provides NB-ARC and CARD-containing proteins (NACs), nucleic acid molecules encoding NACs and antibodies specific for at least one NAC. The invention further provides chimeric NAC proteins. The invention also provides screening assays for identifying an agent that can effectively alter the association of a NAC with a NAC-associated protein. The invention further provides methods of modulating apoptosis in a cell by introducing into the cell a nucleic acid molecule encoding a NAC or an antisense nucleotide sequence. The invention also provides a method of using a reagent that can specifically bind to a NAC to diagnose a pathology that is characterized by an increased or decreased level of apoptosis in a cell.

Non-exemplary Claims: ...acid according to claim 10 effective to inhibit expression of a human NAC and an **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.

5/3,K,AB/8
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10224965 IFI Acc No: 2002-0168672 IFI Acc No: 2002-0043864
Document Type: C
NUCLEIC ACID ENCODING SCHWANNOMIN-BINDING-PROTEINS AND PRODUCTS RELATED THERETO; NUCLEOTIDE SEQUENCES CODING PROTEINS FOR USE IN THE TREATMENT OF TUMORS
Inventors: Pulst Stefan M (US); Scoles Daniel R (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20020168672 20021114 US 2002117604 20020404
Publication Kind: A1
Division Pub(No),Applic(No,Date): US 6376174 US 97971089 19971114
Priority Applic(No,Date): US 2002117604 20020404; US 97971089 19971114
Provisional Applic(No,Date): US 60-30987 19961115

Abstract: In accordance with the present invention, there are provided novel Schwannomin-Binding-Proteins (SBPs). Nucleic acid sequences encoding

such proteins and assays employing same are also disclosed. The invention SBPs can be employed in a variety of ways, for example, for the production of anti-SBP antibodies thereto, in therapeutic compositions and methods employing such proteins and/or antibodies. Also provided are transgenic nonhuman mammals that express the invention protein.

Non-exemplary Claims: ...acid according to claim 11 effective to inhibit expression of a human SBP and an **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.

5/3,K,AB/9
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10220996 IFI Acc No: 2002-0164703 IFI Acc No: 2002-0042781
Document Type: C
CARD-DOMAIN CONTAINING POLYPEPTIDES, ENCODING NUCLEIC ACIDS, AND METHODS OF USE; NUCLEOTIDE SEQUENCES CODING POLYPEPTIDE FOR USE IN THE TREATMENT AND DIAGNOSIS NERVOUS SYSTEM DISORDERS AND INFECTIONS
Inventors: Godzik Adam (US); Pawlowski Krzysztof (SE); Reed John C (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20020164703 20021107 US 200132159 20011219
Publication Kind: A1
Priority Applic(No,Date): US 200132159 20011219
Provisional Applic(No,Date): US 60-257457 20001221

Abstract: The invention provides caspase recruitment domain (CARD)containing polypeptides and functional fragments thereof, encoding nucleic acid molecules, and specific antibodies. Also provided are screening methods for identifying CARD-associated polypeptides (CAPs), and for identifying agents that alter the association of a CARD-containing polypeptide with itself or with a CAP. Further provided are methods of altering a biochemical process modulated by a CARD-containing polypeptide, and methods of diagnosing a pathology characterized by an increased or decreased level of a CARD-containing polypeptide.

Non-exemplary Claims: ...or claim 2(c) effective to inhibit expression of a CARD-containing polypeptide, and an **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.

5/3,K,AB/10
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10217489 IFI Acc No: 2002-0161196 IFI Acc No: 2002-0042106
Document Type: C
TRAIL RECEPTORS NUCLEIC ACIDS ENCODING THE SAME AND METHODS OF USE THEREOF; USEFUL AS IMMUNOGENS FOR PRODUCING ANTI-DR5 OR ANTI-TRAIL-R3 ANTIBODIES, OR IN THERAPEUTIC FORMULATIONS CONTAINING SUCH PROTEINS AND/OR ANTIBODIES; USEFUL IN BIOASSAYS TO IDENTIFY AGONISTS AND ANTAGONISTS
Inventors: Alnemri Emad S (US)
Assignee: Jefferson, Thomas University
Assignee Code: 06943
Publication (No,Date), Applic (No,Date):
US 20020161196 20021031 US 200276773 20020212
Publication Kind: A1

Division Pub(No),Applic(No,Date): PENDING US 98134618
19980814
Priority Applic(No,Date): US 200276773 20020212; US 98134618 19980814
Provisional Applic(No,Date): US 60-55906 19970815

Abstract: In accordance with the present invention, there are provided isolated mammalian TRAIL receptor proteins, antibodies thereto, therapeutic compositions, and nucleic acids encoding such. Bioassays and therapeutic methods employing invention DR5 and TRAIL-R3 proteins are also provided.

Non-exemplary Claims: ...14 effective to inhibit expression of a human DR5 or TRAIL-R3 protein and an **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.

5/3,K,AB/11
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10217488 IFI Acc No: 2002-0161195 IFI Acc No: 2002-0042105
Document Type: C
TRAIL RECEPTORS, NUCLEIC ACIDS ENCODING THE SAME, AND METHODS OF USE THEREOF; USEFUL AS IMMUNOGENS FOR PRODUCING ANTI-DR5 OR ANTI-TRAIL-R3 ANTIBODIES, OR IN THERAPEUTIC FORMULATIONS CONTAINING SUCH PROTEINS AND/OR ANTIBODIES; USEFUL IN BIOASSAYS TO IDENTIFY AGONISTS AND ANTAGONISTS
Inventors: Alnemri Emad S (US)
Assignee: Jefferson, Thomas University
Assignee Code: 06943
Publication (No,Date), Applic (No,Date):
US 20020161195 20021031 US 200276754 20020212
Publication Kind: A1
Division Pub(No),Applic(No,Date): PENDING US 98134618
19980814
Priority Applic(No,Date): US 200276754 20020212; US 98134618 19980814
Provisional Applic(No,Date): US 60-55906 19970815

Abstract: In accordance with the present invention, there are provided isolated mammalian TRAIL receptor proteins, antibodies thereto, therapeutic compositions, and nucleic acids encoding such. Bioassays and therapeutic methods employing invention DR5 and TRAIL-R3 proteins are also provided.

Non-exemplary Claims: ...14 effective to inhibit expression of a human DR5 or TRAIL-R3 protein and an **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.

5/3,K,AB/12
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10171464 IFI Acc No: 2002-0115154 IFI Acc No: 2002-0029569
Document Type: C
TRAIL RECEPTORS, NUCLEIC ACIDS ENCODING THE SAME, AND METHODS OF USE THEREOF; NUCLEOTIDE SEQUENCES CODING MEMBRANE PROTEIN FOR USE IN THE TREATMENT OF ACQUIRED IMMUNODEFICIENCY SYNDROME, NERVOUS SYSTEM DISORDERS, ISCHEMIC INJURY AND AUTOIMMUNE DISEASE
Inventors: Alnemri Emad S (US)
Assignee: Jefferson, Thomas University
Assignee Code: 06943
Publication (No,Date), Applic (No,Date):

US 20020115154 20020822 US 200267615 20020204
Publication Kind: A1
Division Pub(No),Applic(No,Date): PENDING US 98134618 19980814
Priority Applic(No,Date): US 200267615 20020204; US 98134618 19980814
Provisional Applic(No,Date): US 60-55906 19970815

Abstract: In accordance with the present invention, there are provided isolated mammalian TRAIL receptor proteins, antibodies thereto, therapeutic compositions, and nucleic acids encoding such. Bioassays and therapeutic methods employing invention DR5 and TRAIL-R3 proteins are also provided.

Non-exemplary Claims: ...14 effective to inhibit expression of a human DR5 or TRAIL-R3 protein and an **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.

5/3,K,AB/13
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10171459 IFI Acc No: 2002-0115149 IFI Acc No: 2002-0029564
Document Type: C
DNA ENCODING HUMAN 5-HT1D RECEPTORS AND USES THEREOF; NUCLEOTIDE SEQUENCES CODING MEMBRANE PROTEIN FOR USE IN THE TREATMENT OF PARKINSON'S DISEASE, EATING DISORDERS, TENSION AND HEADACHES
Inventors: Branchek Theresa (US); Hartig Paul R (US); Weinshank Richard L (US)
Assignee: Synaptic Pharmaceutical Corp
Assignee Code: 34644
Publication (No,Date), Applic (No,Date):
US 20020115149 20020822 US 20015010 20011029
Publication Kind: A1
Continuation Pub(No),Applic(No,Date): ABANDONED US 93946364 19930108; GRANTED US 95461812 19950605; PENDING US 99371705 19990809
Section 371 Pub(No,Date),Applic(No,Date):US 93946364 19930108;WO 91US3200 19910508
Priority Applic(No,Date): US 20015010 20011029; US 93946364 19930108; US 95461812 19950605; US 99371705 19990809

Abstract: This invention provides isolated nucleic acid molecules encoding human 5-HT1D receptors, isolated proteins which are human 5HT1D receptors, vectors comprising isolated nucleic acid molecules encoding human 5-HT1D receptors, mammalian cells comprising such vectors, antibodies directed to the human 5HT1D receptors, nucleic acid probes useful for detecting nucleic acid encoding human 5-HT1D receptors, antisense oligonucleotides complementary to any sequences of a nucleic acid molecule which encodes a human 5-HT1D receptor, pharmaceutical compounds related to human 5-HT1D receptors, and nonhuman transgenic animals which express DNA a normal or a mutant human 5-HT1D receptor. This invention further provides methods for determining ligand binding, detecting expression, drug screening, and treatment involving the human 5-HT1D receptor.

Non-exemplary Claims: ...oligonucleotide of claim 32 effective to reduce expression of a human 5-HT1D receptor by **passing** through a **cell membrane** and binding specifically with mRNA encoding a human 5-HT1D receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.
...

...39. A pharmaceutical composition of claim 36, wherein the pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane** comprises a structure which binds to a receptor specific for a selected cell type and

5/3,K,AB/14
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10163131 IFI Acc No: 2002-0106778 IFI Acc No: 2002-0027504
Document Type: C
HUMAN PTTG POLYPEPTIDE AND METHOD FOR PRODUCING IT; PURIFIED PROTEIN FOR USE IN THE TREATMENT OF TMORS
Inventors: Melmed Shlomo (US); Pei Lin (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20020106778 20020808 US 2001949272 20010907
Publication Kind: A1
Continuation Pub(No),Applic(No,Date): PENDING US 99894251 19990723
Section 371 Pub(No,Date),Applic(No,Date):US 99894251 19990723;WO 97US21463 19971121
Priority Applic(No,Date): US 2001949272 20010907; US 99894251 19990723
Provisional Applic(No,Date): US 60-31338 19961121

Abstract: Polypeptides are expressed by the pituitary-tumor-transforminggene (PTTG), formerly known as pituitary-tumor-specific-gene (PTSG), and nucleic acids encode them. Examples are the human and rat PTTG proteins. The nucleic acids may be applied to the production of a recombinant protein, and to the detection of the presence of PTTG genes in different species. The nucleic acids may be operatively linked to a vector, optionally provided with control and expression sequences and/or being carried by a host cell. The nucleic acids may also be delivered to a mammal to compensate for the absence, or a defective expression, of endogenous protein. The nucleic acids, proteins, and antibodies are also employed in disgnostic assays, as well as, for example, in the production of anti-PTTG antibodies (protein), therapeutic compositions and other applications of the proteins and antibodies. Various kits utilize nucleic acids, polypeptides, and/or antibodies. A transgenic non-human mammal expresses PTTG.

Non-exemplary Claims: ...to claim 32, effective to inhibit expression of a human PTTG gene, and a pharmaceutically **acceptable hydrophobic carrier** which **passing** through a **cell membrane**.

5/3,K,AB/15
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10143204 IFI Acc No: 2002-0086845 IFI Acc No: 2002-0022673
Document Type: C
RAT PTTG POLYPEPTIDE AND METHOD FOR PRODUCING IT; PITUITARY TUMOR TRANSFORMING GENE (PTTG), FORMERLY PITUITARY TUMOR SPECIFIC GENE (PTTG)
Inventors: Melmed Shlomo (US); Pei Lin (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):

US 20020086845 20020704 US 2001949270 20010907
Publication Kind: A1
Division Pub(No),Applic(No,Date): PENDING US 99894251 19990723
Section 371 Pub(No,Date),Applic(No,Date):US 99894251 19990723;WO 97US21463 19971121
Priority Applic(No,Date): US 2001949270 20010907; US 99894251 19990723
Provisional Applic(No,Date): US 60-31338 19961121

Abstract: Polypeptides are expressed by the pituitary-tumor-transforminggene (PTTG), formerly known as pituitary-tumor-specific-gene (PTTG), and nucleic acids encode them. Examples are the human and rat PTTG proteins. The nucleic acids may be applied to the production of a recombinant protein, and to the detection of the presence of PTTG genes in different species. The nucleic acids may be operatively linked to a vector, optionally provided with control and expression sequences and/or being carried by a host cell. The nucleic acids may also be delivered to a mammal to compensate for the absence, or a defective expression, of endogenous protein. The nucleic acids, proteins, and antibodies are also employed in disgnostic assays, as well as, for example, in the production of anti-PTTG antibodies (protein), therapeutic compositions and other applications of the proteins and antibodies. Various kits utilize nucleic acids, polypeptides, and/or antibodies. A transgenic non-human mammal expresses PTTG.

Non-exemplary Claims: ...to claim 32, effective to inhibit expression of a human PTTG gene, and a pharmaceutically **acceptable hydrophobic carrier** which **passing** through a **cell membrane**.

5/3,K,AB/16
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10138036 IFI Acc No: 2002-0081661 IFI Acc No: 2002-0021291
Document Type: C
DNA ENCODING 5-HT4 SEROTONIN RECEPTORS AND USES THEREOF; NUCLEOTIDE SEQUENCES CODING PREFERENTIAL POLYPEPTIDE FOR USE IN COGNITIVE ENHANCEMENT; FOR USE IN TREATING DIABETES AND GASTROINTESTINAL DISORDER
Inventors: Branchek Theresa A (US); Gerald Christophe P G (US); Hartig Paul R (US); Weinshank Richard L (US)
Assignee: Synaptic Pharmaceutical Corp
Assignee Code: 34644
Publication (No,Date), Applic (No,Date):
US 20020081661 20020627 US 2001989861 20011119
Publication Kind: A1
Continuation Pub(No),Applic(No,Date): GRANTED US 98328314 19980403
Division Pub(No),Applic(No,Date): GRANTED US 95446822 19950731
Section 371 Pub(No,Date),Applic(No,Date):US 95446822 19950731;WO 93US12586 19931222
Priority Applic(No,Date): US 2001989861 20011119; US 98328314 19980403; US 95446822 19950731
Abstract: This invention provides an isolated nucleic acid molecule encoding a mammalian 5-HT4 receptor and an isolated nucleic acid molecule encoding a human 5-HT4 receptor, an isolated protein which is a mammalian 5-HT4 receptor, an isolated protein which is a human 5-HT4 receptor, vectors comprising an isolated nucleic acid molecule encoding a mammalian 5-HT4 receptor, vectors comprising and isolated nucleic acid molecule encoding a human 5-HT4 receptor, mammalian cells comprising such vectors, antibodies directed to the 5-HT4 receptor, nucleic acid probes useful for

detecting nucleic acid encoding a mammalian or human 5-HT4 receptor, antisense oligonucleotides complementary to any sequences of a nucleic acid molecule which encodes a mammalian or human 5-HT4 receptor, pharmaceutical compounds related to the human 5-HT4 receptor, and nonhuman transgenic animals which express DNA encoding a normal or a mutant mammalian or human 5-HT4 receptor. This invention further provides methods for determining ligand binding, detecting expression, drug screening, and treatments for alleviating abnormalities associated with a human 5-HT4 receptor.

Non-exemplary Claims: ...oligonucleotide of claim 31 effective to reduce expression of a human 5-HT4 receptor by **passing** through a **cell membrane** and specifically binding with mRNA encoding a human 5-HT4 receptor in the cell so as to prevent its translation and a pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.
...

...60. A pharmaceutical composition of claim 58, wherein the pharmaceutically **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane** comprises a structure which binds to a transporter specific for a selected cell type and...mammal, which plasmid further comprises DNA which expresses a human 5-HT4 receptor on the **cell**'s surface, isolating a **membrane** fraction from the **cell** extract, incubating the compound with the membrane fraction under conditions permitting binding of ligands known...

...cell which plasmid further comprises DNA which expresses a human 5-HT4 receptor on the **cell**'s surface, isolating a **membrane** fraction from the **cell** extract, incubating the **membrane** fraction with a plurality of compounds, determining those compounds which interact with and bind to...

5/3,K,AB/17
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 10125102 IFI Acc No: 2002-0068716 IFI Acc No: 2002-0018698
Document Type: C
COMPOSITIONS AND METHOD FOR DETERMINING THE PRESENCE OF RAT PTTG PEPTIDE IN A SAMPLE; PITUITARY-TUMOR-TRANSFORMING-GENE (PTTG) POLYPEPTIDE EXPRESSED BY PITUITARY TUMOR CELLS, WHICH BINDS ANTI-PTTG ANTIBODY.
Inventors: Melmed Shlomo (US); Pei Lin (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20020068716 20020606 US 2001949271 20010907
Publication Kind: A1
Division Pub(No),Applic(No,Date): PENDING US 99894251 19990723
Section 371 Pub(No,Date),Applic(No,Date):US 99894251 19990723;WO 97US21463 19971121
Priority Applic(No,Date): US 2001949271 20010907; US 99894251 19990723
Provisional Applic(No,Date): US 60-31338 19961121

Abstract: Polypeptides are expressed by the pituitary-tumor-transforminggene (PTTG), formerly known as pituitary-tumor-specific-gene (PTSG), and nucleic acids encode them. Examples are the human and rat PTTG proteins. The nucleic acids may be applied to the production of a recombinant protein, and to the detection of the presence of PTTG genes in different species. The nucleic acids may be operatively linked to a vector, optionally provided with control and

expression sequences and/or being carried by a host cell. The nucleic acids may also be delivered to a mammal to compensate for the absence, or a defective expression, of endogenous protein. The nucleic acids, proteins, and antibodies are also employed in disgnostic assays, as well as, for example, in the production of anti-PTTG antibodies (protein), therapeutic compositions and other applications of the proteins and antibodies. Various kits utilize nucleic acids, polypeptides, and/or antibodies. A transgenic non-human mammal expresses PTTG.

Non-exemplary Claims: ...to claim 32, effective to inhibit expression of a human PTTG gene, and a pharmaceutically **acceptable hydrophobic carrier** which **passing** through a **cell membrane**.

5/3,K,AB/18
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2004 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 10124740 IFI Acc No: 2002-0068353 IFI Acc No: 2002-0018539
Document Type: C
COMPOSITIONS AND METHOD FOR DETERMINING THE PRESENCE OF HUMAN PTTG PEPTIDE IN A SAMPLE; NUCLEOTIDE SEQUENCE CODING TUMOR POLYPEPTIDE FOR USE AS ANTICARCINOGENEIC AGENTS
Inventors: Melmed Shlomo (US); Pei Lin (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20020068353 20020606 US 2001949476 20010907
Publication Kind: A1
Division Pub(No),Applic(No,Date): PENDING US 99894251 19990723
Section 371 Pub(No,Date),Applic(No,Date):US 99894251 19990723;WO 97US21463 19971121
Priority Applic(No,Date): US 2001949476 20010907; US 99894251 19990723
Provisional Applic(No,Date): US 60-31338 19961121

Abstract: Polypeptides are expressed by the pituitary-tumor-transforminggene (PTTG), formerly known as pituitary-tumor-specific-gene (PTSG), and nucleic acids encode them. Examples are the human and rat PTTG proteins. The nucleic acids may be applied to the production of a recombinant protein, and to the detection of the presence of PTTG genes in different species. The nucleic acids may be operatively linked to a vector, optionally provided with control and expression sequences and/or being carried by a host cell. The nucleic acids may also be delivered to a mammal to compensate for the absence, or a defective expression, of endogenous protein. The nucleic acids, proteins, and antibodies are also employed in disgnostic assays, as well as, for example, in the production of anti-PTTG antibodies (protein), therapeutic compositions and other applications of the proteins and antibodies. Various kits utilize nucleic acids, polypeptides, and/or antibodies. A transgenic non-human mammal expresses PTTG.

Non-exemplary Claims: ...to claim 32, effective to inhibit expression of a human PTTG gene, and a pharmaceutically **acceptable hydrophobic carrier** which **passing** through a **cell membrane**.

5/3,K,AB/19
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2004 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 3936673 IFI Acc No: 0033956
Document Type: C
(A1) NUCLEIC ACIDS ENCODING ATAXIN-2 BINDING PROTEINS, PRODUCTS RELATED THERETO AND METHODS OF USING SAME; GENETIC ENGINEERING
(B) ATAXIN-2 BINDING PROTEINS
Inventors: Pulst Stefan M (US); Shibata Hiroki (US)
Assignee: (A1) Cedars-Sinai Medical Center
(B) Cedars-Sinai Medical Center
Assignee Code: (A1) 11053; (B) 11053
Publication (Kind,No,Date), Applic (No,Date):
US A1 US 20010018198 20010830 US 2001794591 20010226
US B US 6617430 20030909 US 2001794591 20010226
Division Pub(No),Applic(No,Date): US 6194171 US 98145391 19980901
Priority Applic(No,Date): US 2001794591 20010226; US 98145391 19980901

Abstract: (US 20010018198 A1)
In accordance with the present invention, there are provided novel isolated nucleic acids encoding ataxin-2-binding proteins (A2BPs), functional fragments thereof, vectors containing invention nucleic acids and recombinant cells transformed therewith, antisense-nucleic acids thereto. Also provided are novel isolated ataxin-2-binding proteins (A2BPs) having ability to bind to ataxin-2, methods for expression of A2BP, transgenic non-human mammals that express invention A2BP, anti-A2BP antibodies, and methods related thereto.

Abstract: (US 6617430 B)
In accordance with the present invention, there are provided novel isolated nucleic acids encoding ataxin-2-binding proteins (A2BPs), functional fragments thereof, vectors containing invention nucleic acids and recombinant cells transformed therewith, antisense-nucleic acids thereto. Also provided are novel isolated ataxin-2-binding proteins (A2BPs) having ability to bind to ataxin-2, methods for expression of A2BP, transgenic non-human mammals that express invention A2BP, anti-A2BP antibodies, and methods related thereto.

Non-exemplary Claims: ...claim 13 in an amount effective to inhibit expression of a human A2BP and an **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.

5/3,K,AB/20
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 3715455 IFI Acc No: 0223916
Document Type: C
(A1) NOVEL TRAIL RECEPTORS, NUCLEIC ACIDS ENCODING SAME, AND METHODS OF USE THEREOF; ISOLATED GENES ENCODING TUMOR NECROSIS FACTOR-RELATED APOTOSIS-INDUCING LIGAND (TRAIL) RECEPTOR SPLICE VARIANT CDNA SEQUENCES, OR ACTIVE FRAGMENT; IMMUNOGENS, MODULATION THERAPEUTIC AUTOIMMUNE DISEASES, AIDS
(B) TRAIL RECEPTORS, NUCLEIC ACIDS ENCODING THE SAME, AND METHODS OF USE THEREOF; ISOLATED GENES ENCODING TUMOR NECROSIS FACTOR-RELATED APOTOSIS-INDUCING LIGAND (TRAIL) RECEPTOR SPLICE VARIANT CDNA SEQUENCES, OR ACTIVE FRAGMENT; IMMUNOGENS, MODULATION THERAPEUTIC AUTOIMMUNE DISEASES, AIDS
Inventors: Alnemri Emad S (US)
Assignee: (A1) Unassigned Or Assigned To Individual
(B) Jefferson, Thomas University
Assignee Code: (A1) 68000; (B) 06943

Publication (Kind,No,Date), Applic (No,Date):
US A1 US 20010029030 20011011 US 98134618 19980814
US B US 6417328 20020709 US 98134618 19980814
Calculated Expiration: 20180814
Priority Applic(No,Date): US 98134618 19980814

Abstract: (US 20010029030 A1)
In accordance with the present invention, there are provided isolated mammalian TRAIL receptor proteins, antibodies thereto, therapeutic compositions, and nucleic acids encoding such. Bioassays and therapeutic methods employing invention DR5 and TRAIL-R3 proteins are also provided.

Abstract: (US 6417328 Granted)
In accordance with the present invention, there are provided isolated mammalian TRAIL receptor proteins, antibodies thereto, therapeutic compositions, and nucleic acids encoding such. Bioassays and therapeutic methods employing invention DR5 and TRAIL-R3 proteins are also provided.

Non-exemplary Claims: ...14 effective to inhibit expression of a human DR5 or TRAIL-R3 protein and an **acceptable hydrophobic carrier** capable of **passing** through a **cell membrane**.
?

08498177 Genuine Article#: 292VU Number of References: 47
Title: Subcellular localization and **CARD**-dependent oligomerization of the death adaptor RAIDD (ABSTRACT AVAILABLE)
Author(s): ShearwinWhyatt LM; Harvey NL; Kumar S (REPRINT)
Corporate Source: IMVS,HANSON CTR CANC RES, POB 14, RUNDLE MALL, FROME RD/ADELAIDE/SA 5000/AUSTRALIA/ (REPRINT); IMVS,HANSON CTR CANC RES/ADELAIDE/SA 5000/AUSTRALIA/; UNIV ADELAIDE,DEPT MED/ADELAIDE/SA 5005/AUSTRALIA/
Journal: CELL DEATH AND DIFFERENTIATION, 2000, V7, N2 (FEB), P155-165
ISSN: 1350-9047 Publication date: 20000200
Publisher: STOCKTON PRESS, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND
Language: English Document Type: ARTICLE
Abstract: RAIDD, a caspase recruitment domain (**CARD**) containing molecule, interacts with procaspase-2 in a **CARD**-dependent manner, This interaction has been suggested to mediate the recruitment of caspase-2 to the tumour necrosis factor receptor 1 (TNFR1), In this paper we have studied the subcellular localization of RAIDD and its interaction with caspase-2, We demonstrate that endogenous RAIDD is mostly localized in the cytoplasm and to some extent in the nucleus. RAIDD localization is not affected by TNF-treatment of HeLa cells, but in cells ectopically expressing caspase-2, a fraction of RAIDD is recruited to the nucleus. In transfected cells, coexpression of RAIDD and caspase-2 leads to **CARD**-dependent colocalization of the two proteins to discrete subcellular structures. We further show that overexpression of the RAIDD-**CARD** results in the formation of filamentous structures due to **CARD**-mediated oligomerization, These structures were similar to death effector filaments (DEFs) formed by FADD and FLICE death effector domains (DEDs), and partially colocalized with DEFs, Our results suggest that similar to the DED, the RAIDD-**CARD** has the ability to form higher order complexes, believed to be important in apoptotic execution. We also present evidence that RAIDD-**CARD** oligomerization may be regulated by intramolecular folding of the RAIDD molecule.

09926706 Genuine Article#: 464XE Number of References: 50
Title: The adapter protein apoptotic protease-**activating** factor-1 (Apaf-1) is proteolytically processed during apoptosis (ABSTRACT AVAILABLE)
Author(s): Lauber K; Appel HAE; Schlosser SF; Gregor M; Schulze-Osthoff K; Wesselborg S (REPRINT)
Corporate Source: Univ Tubingen,Dept Internal Med 1,Otfried Muller Str 10/D-72076 Tubingen//Germany/ (REPRINT); Univ Tubingen,Dept Internal Med 1,D-72076 Tubingen//Germany/; Univ Munster,Dept Immunol & Cell Biol,D-48149 Munster//Germany/
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 2001, V276, N32 (AUG 10), P 29772-29781
ISSN: 0021-9258 Publication date: 20010810
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA
Language: English Document Type: ARTICLE
Abstract: Apoptotle protease-**activating** factor-1 (Apaf-1), a key regulator of the mitochondrial apoptosis pathway, consists of three functional regions. (i) an N-terminal caspase recruitment domain (**CARD**) that can bind to procaspase-9, (ii) a CED-4-like region enabling self-oligomerization, and (iii) a regulatory C terminus with WD-40 repeats masking the **CARD** and CED-4 region. During apoptosis, cytochrome c and dATP can relieve the inhibitory action of the WD-40 repeats and thus enable the oligomerization of Apaf-1 and the subsequent recruitment and **activation** of procaspase-9. Here, we report that different apoptotic stimuli induced the caspase-mediated cleavage of Apaf-1 into an 84-kDa fragment. The same Apaf-1 fragment was obtained in vitro by incubation of cell lysates with either cytochrome c/dATP or caspase-3 but not with caspase-6 or caspase-8. Apaf-1 was cleaved at the N terminus, leading to the removal of its **CARD** HI helix. An additional cleavage site was located within the WD-40 repeats and enabled the oligomerization of p84 into a similar to 440-kDa Apaf-1 multimer even in the absence of cytochrome c. Due to the partial loss of its **CARD**, the p84 multimer was devoid of caspase-9 or other caspase activity. Thus, our data indicate that Apaf-1 cleavage causes the release of caspases from the apoptosome in the course of apoptosis.

Title: The adapter protein apoptotic protease-**activating** factor-1 (Apaf-1) is proteolytically processed during apoptosis
Abstract: Apoptotle protease-**activating** factor-1 (Apaf-1), a key regulator of the mitochondrial apoptosis pathway, consists of three functional regions. (i) an N-terminal caspase recruitment domain (**CARD**) that can bind to procaspase-9, (ii) a CED-4-like region enabling self-oligomerization, and (iii) a regulatory C terminus with WD-40 repeats masking the **CARD** and CED-4 region. During apoptosis, cytochrome c and dATP can relieve the inhibitory action...

...40 repeats and thus enable the oligomerization of Apaf-1 and the subsequent recruitment and **activation** of procaspase-9. Here, we report that different apoptotic stimuli induced the caspase-mediated cleavage...

...8. Apaf-1 was cleaved at the N terminus, leading to the removal of its **CARD** HI helix. An additional cleavage site was located within the WD-40 repeats and enabled...

...multimer even in the absence of cytochrome c. Due to the partial loss of its **CARD**, the p84 multimer was devoid of caspase-9 or other caspase activity. Thus, our data...
...Identifiers--DRUG-INDUCED APOPTOSIS; WD-40 REPEAT REGION; CYTOCHROME-C; CASPASE **ACTIVATION**; CELL-DEATH; PROCASPASE-9 **ACTIVATION**; BCL-2 FAMILY; COMPLEX; **CASPASE**-8/FLICE; **OLIGOMERIZATION**

17/3,K,AB/12 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09533581 Genuine Article#: 416UK Number of References: 26
Title: Apaf-1XL is an inactive isoform compared with Apaf-1L

17/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11443760 PMID: 11432859
Cop, a caspase recruitment domain-containing protein and inhibitor of caspase-1 **activation** processing.
Lee S H; Stehlik C; Reed J C
Burnham Institute, La Jolla, California 92037, USA.
Journal of biological chemistry (United States) Sep 14 2001, 276 (37) p34495-500, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: GM61694; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The production of bio-active interleukin-1beta (IL-1beta), a pro-inflammatory cytokine, is mediated by **activated** caspase-1. One of the known molecular mechanisms underlying pro-caspase-1 processing and **activation** involves binding of the caspase-1 prodomain to a caspase recruitment domain (**CARD**)-containing serine/threonine kinase known as RIP2/CARDIAK/RICK. We have identified a novel protein, COP (**CARD** only protein), which has a high degree of sequence identity to the caspase-1 prodomain. COP binds to both RIP2 and the caspase-1 prodomain and inhibits RIP2-induced **caspase**-1 **oligomerization**. COP inhibits **caspase** - 1-induced IL-1beta secretion as well as lipopolysaccharide-induced IL-1beta secretion in transfected cells. Our data indicate that COP can regulate IL-1beta secretion, implying that COP may play a role in down-regulating inflammatory responses analogous to the **CARD** protein ICEBERG.

Cop, a caspase recruitment domain-containing protein and inhibitor of caspase-1 **activation** processing.
... production of bio-active interleukin-1beta (IL-1beta), a pro-inflammatory cytokine, is mediated by **activated** caspase-1. One of the known molecular mechanisms underlying pro-caspase-1 processing and **activation** involves binding of the caspase-1 prodomain to a caspase

17/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11751822 PMID: 11904389

Oligomerization and **activation** of **caspase**-9, induced by Apaf-1 **CARD**.

Shiozaki Eric N; Chai Jijie; Shi Yigong

Department of Molecular Biology, Princeton University, Lewis Thomas Laboratory, Washington Road, Princeton, NJ 08544, USA.

Proceedings of the National Academy of Sciences of the United States of America (United States) Apr 2 2002, 99 (7) p4197-202, ISSN 0027-8424 Journal Code: 7505876

Contract/Grant No.: R01-CA90269; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Apaf-1 facilitates the proteolytic **activation** of procaspase-9 and maintains the hyperactive state of the processed caspase-9. The underlying molecular mechanisms for these activities remain poorly characterized. Here we report that the isolated Apaf-1 caspase recruitment domain (**CARD**) forms a large hetero-**oligomer** with the active **caspase**-9. The catalytic activity of caspase-9 is significantly enhanced in this complex, demonstrating that Apaf-1 **CARD** allosterically up-regulates caspase-9 activity. Point mutations that inactivate the interactions between Apaf-1 **CARD** and the prodomain of caspase-9 also abolished the formation of this complex. Based on these observations, we discuss the implications of this complex on the observed Apaf-1 function.

Oligomerization and **activation** of **caspase**-9, induced by Apaf-1 **CARD**.

Apaf-1 facilitates the proteolytic **activation** of procaspase-9 and maintains the hyperactive state of the processed caspase-9. The underlying

2128877 PMID: 12459189

Nod1, a **CARD** protein, enhances pro-interleukin-1beta processing through the interaction with pro-caspase-1.

Yoo Nam Jin; Park Won Sang; Kim Su Young; Reed John C; Son Seong Gon; Lee Jung Young; Lee Sug Hyung

Department of Pathology, College of Medicine, The Catholic University of Korea, 505 Banpo-dong, Socho-gu, Seoul 137-701, South Korea.

Biochemical and biophysical research communications (United States) Dec 13 2002, 299 (4) p652-8, ISSN 0006-291X Journal Code: 0372516

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The production of bioactive interleukin-1beta (IL-1beta), a pro-inflammatory cytokine, is mediated by **activated** caspase-1. One of the known molecular mechanisms underlying pro-caspase-1 processing and **activation** involves interaction between the caspase recruit domains (CARDs) of caspase-1 and a serine/threonine kinase RIP2. While the association of Nod1 with both caspase-1 and RIP2 is already known, the consequences of these interactions are poorly understood. Because Nod1 also binds to RIP2, we hypothesized that Nod1 plays a role in pro-caspase-1 **activation** and IL-1beta processing. We show here that Nod1 binds to both RIP2 and caspase-1 by **CARD** interactions. Nod1 enhances pro-**caspase**-1 **oligomerization** and pro-**caspase**-1 processing. Nod1 enhances caspase-1-induced IL-1beta secretion, as well as lipopolysaccharide (LPS)-induced IL-1beta secretion in transfected cells. Moreover, HT1080 cells stably transfected with Nod1 showed higher LPS-induced IL-1beta secretion than non-transfected cells, suggesting a role of Nod1 in LPS-induced responses. Our data indicate that Nod1 can regulate IL-1beta secretion, implying that Nod1 may play a role in inflammatory responses to bacterial LPS.

from 60/181,159

```
M   G   E   L   C   R   R   D   S   A   L   T   A   L   D   E   E   T   L   W     20
ATG GGG GAA CTG TGC CGC AGG GAC TCC GCA CTC ACG GCA CTG GAC GAG GAG ACA CTG TGG   60

E   M   M   E   S   H   R   H   R   I   V   R   C   I   C   P   S   R   L   T     40
GAG ATG ATG GAG AGC CAC CGC CAC AGG ATC GTA CGC TGC ATC TGC CCC AGC CGC CTC ACC  120

P   Y   L   R   Q   A   K   V   L   C   Q   L   D   E   E   E   V   L   H   S     60
CCC TAC CTG CGC CAG GCC AAG GTG CTG TGC CAG CTG GAC GAG GAG GAG GTG CTG CAC AGC  180

P   R   L   T   N   S   A   M   R   A   G   H   L   L   D   L   L   K   T   R     80
CCC CGG CTC ACC AAC AGC GCC ATG CGG GCC GGG CAC TTG CTG GAT TTG CTG AAG ACT CGA  240

G   K   N   G   A   I   A   F   L   E   S   L   K   F   H   N   P   D   V   Y    100
GGG AAG AAC GGG GCC ATC GCC TTC CTG GAG AGC CTG AAG TTC CAC AAC CCT GAC GTC TAC  300

T   L   V   T   G   L   Q   P   D   V   D   F   S   N   F   S   G   E   S   S    120
ACC CTG GTC ACC GGG CTG CAG CCT GAT GTT GAC TTC AGT AAC TTT AGC GGT GAG AGC TCC  360

D   F   D   G   L   A   G   T   S   R   N   L   R   L   L   V   T   P   G   L    140
GAC TTT GAC GGT TTG GCA GGC ACT TCT AGG AAC CTC AGG CTC CTG GTA ACC CCA GGT CTC  420

M   E   T   S   K   L   T   E   C   L   A   G   A   I   G   S   L   Q   E   E    160
ATG GAG ACA TCC AAG CTG ACC GAG TGC CTG GCT GGG GCC ATC GGC AGC CTG CAG GAG GAG  480

L   N   Q   E   K   G   Q   K   E   V   L   L   R   R   C   Q   Q   L   Q   E    180
CTG AAC CAG GAA AAG GGG CAG AAG GAG GTG CTG CTG CGG CGG TGC CAG CAG CTG CAG GAG  540

H   L   G   L   A   E   T   R   A   E   G   L   H   Q   L   E   A   D   H   S    200
CAC CTG GGC CTG GCC GAG ACC CGT GCC GAG GGC CTG CAC CAG CTG GAG GCT GAC CAC AGC  600

R   M   K   R   E   V   S   A   H   F   H   E   V   L   R   L   K   D   E   M    220
CGC ATG AAG CGT GAG GTT AGC GCA CAC TTC CAT GAG GTG CTG AGG CTG AAG GAC GAG ATG  660

L   S   L   S   L   H   Y   S   N   A   L   Q   E   K   E   L   A   A   S   R    240
CTC AGC CTC TCG CTG CAC TAT AGC AAT GCG CTG CAG GAG AAG GAG CTG GCC GCC TCA CGC  720

C   R   S   L   Q   E   E   L   Y   L   L   K   Q   E   L   Q   R   A   N   M    260
TGC CGC AGC CTG CAG GAG GAG CTG TAT CTA CTG AAG CAG GAG CTG CAG CGA GCC AAC ATG  780

V   S   S   C   E   L   E   L   Q   E   Q   S   L   R   T   A   S   D   Q   E    280
GTT TCC TCC TGT GAG CTG GAA TTG CAA GAG CAG TCC CTG AGG ACA GCC AGC GAC CAG GAG  840

S   G   D   E   E   L   N   R   L   K   E   E   N   E   K   L   R   S   L   T    300
TCC GGG GAT GAG GAG CTG AAC CGC CTG AAG GAG GAG AAT GAG AAA CTG CGC TCG CTG ACT  900

F   S   L   A   E   K   D   I   L   E   Q   S   L   D   E   A   R   G   S   R    320
TTC AGC CTG GCG GAG AAG GAC ATT CTG GAG CAG AGC CTG GAC GAG GCG CGG GGG AGC CGA  960

Q   E   L   V   E   R   I   H   S   L   R   E   R   A   V   A   A   E   R   Q    340
CAG GAG CTG GTG GAG CGC ATC CAC TCG CTG CGG GAG CGG GCC GTG GCT GCC GAG AGG CAG 1020

R   E   Q   A   R   P   S   E   L   L   S   F   T   V   H   V   S   H   S   V    360
CGA GAG CAG GCC AGA CCC TCA GAG CTG CTG AGC TTC ACG GTC CAT GTG TCC CAC TCT GTC 1080

Q   Y   W   E   E   K   E   Q   T   L   L   Q   F   Q   K   S   K   M   A   C    380
CAG TAC TGG GAA GAG AAG GAA CAG ACC CTG CTG CAG TTC CAG AAG AGT AAG ATG GCC TGC 1140

Q   L   Y   R   E   K   V   N   A   L   Q   A   Q   V   C   E   L   Q   K   E    400
CAA CTC TAC AGG GAG AAG GTG AAT GCG CTG CAG GCC CAG GTG TGC GAG CTG CAG AAG GAG 1200

R   D   Q   A   Y   S   A   R   D   S   A   Q   R   E   I   S   Q   S   L   V    420
CGA GAC CAG GCG TAC TCC GCG AGG GAC AGT GCT CAG AGG GAG ATT TCC CAG AGC CTG GTG 1260

E   K   D   S   L   R   R   Q   V   F   E   L   T   D   Q   V   C   E   L   R    440
GAG AAG GAC TCC CTC CGC AGG CAG GTG TTC GAG CTG ACG GAC CAG GTC TGC GAG CTG CGC 1320

T   Q   L   R   Q   L   Q   A   E   P   P   G   V   L   K   Q   E   A   R   T    460
ACA CAG CTT CGC CAG CTG CAG GCA GAG CCT CCG GGT GTG CTC AAG CAG GAA GCC AGG ACC 1380
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Fig. 1A same as Fig 2A of 2002/0081634 A1

Subject: Rush search request for 10/032159 114184

Please search in commercial database, issued patent files, PGPUB and interference:
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3) Fragments of SEQ ID NO:15, wherein said fragments are different from SEQ ID NO: 19, 21-37.
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